Direct Medical Cost of Children and Adolescents Epilepsy at a University Setting in Croatia

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A B S T R A C T

The aim was to study the direct medical cost of epilepsy in children and adolescents and to determine the impact of epilepsy type and child's age on total costs of treatment.

One-year prospective, prevalence based, »bottom up« analyses of sixty-nine (69) children with epilepsy (International League Against Epilepsy criteria was used). Direct medical costs were calculated by summing annual costs of hospital care, outpatient visits and antiepileptic drug (AED) treatment. The average annual cost per patient was 1293.0 €. The costs of hospital admissions were 942.9 € (72%), followed by drug treatment 240.0 € (19%) and outpatient medical services 121.2 € (9%). The costs of epilepsy were significantly higher for children under 5 year of age. AED costs were statistically significantly lower for children who received traditional AED (€122.0) than modern AED (571.2€). The costs of epilepsy in children and adolescents in Croatia are congruent to those of developed countries. Costs significantly varied regarding the child's age. The cost of illness studies are an important first step towards the rational use of available resources.

Key words: *epilepsy, cost, children, adolescents*

Introduction

The overall medical progress and emerging new treatments in the filed of epilepsy might greatly increase medical cost of the disease, quite often without evident or substantial benefit to the patients[1,2]. In countries with limited health system resources reasonable and more cautioned approach is essential.

There is a general opinion that better understanding of economic aspect of epilepsy leads to the further development of the medical care[3]. Studies on epilepsy costs are scarce regarding children and adolescents population, no matter of higher incidences of epilepsy[4–7].

In Croatia there are only speculations about the expenditures for chronic diseases as well as for epilepsy. Treatment algorithms for most diseases are still developing as well as attention about the cost-benefit ratio or cost-of-illness studies.

We calculated the direct medical costs of epilepsy in children and adolescents to find out which health resource is mostly consumed as the first step towards the rationalized use. Additionally, we wanted to study the impact of the child's age and epilepsy type on the total cost of childhood epilepsy.

Patients and Methods

We performed prospective, prevalence based »bottom--up« analysis of direct medical costs of epilepsy in children and adolescents. All patients were hospitalized at the Department of Paediatrics and Department of Neurology in University Hospital Centre Rijeka. The institution is tertiary medical centre, 1200-bed hospital, the second large in Croatia. It provides medical care for 500 000 inhabitants of the Northern Adriatic region with its surroundings. The patients were prospectively followed up for one consecutive year from the establishing of diagnosis. Data were collected from hospital and outpatients ac-

counting services during the two phases – April 2002-April 2003, and September 2003-September 2004 to gain better internal and external reproducibility. Statistically significant differences between the two periods were not found. Presented results were the average values for these two periods.

Patients

The eligible patients were residents of the UCH Rijeka catchments area. They were followed up for one year upon the first diagnosis of epilepsy. Their epilepsy fulfilled the standard ILAE diagnostic criteria[8] or had clinical and/or EEG evidence of a specific type of epilepsy. The age of children varied from 3 months to 18 years. Neonatal convulsions were not included in the study.

Patients were grouped into categories regarding age: 5 years or under, from 6 to 10 years and from 11 to 18 years. Furthermore, regarding the epilepsy type population was divided in to – general, partial (with or without secondary generalization) or unclassified.

Cost calculations

Unit costs calculations were done following the National Health Service-NHS (Croatian Institute for Health Insurance) regulative. Cost calculations were summed up for each medical or diagnostic procedure, as well as for antiepileptic drugs (AED). The price of a medical procedure (hospital care, outpatient visits, laboratory tests, diagnostic procedure, medical materials, etc) was defined by NHS[9,10]. The price of consumed medical resources was taken from the actual hospital invoice toward the NHS, thus calculated costs represented factual expenses.

Direct medical expenditures related to epilepsy were gained from the UHC Rijeka computer account data system. The unit cost of resource was calculated using the NHS tariffs indicated in Euros (€) by official exchange rate at the study period.

Consumption of resources

Total costs were calculated by summing resources consumed through one of three main costs categories (hospital or outpatient or AED). In cooperation, total, average and per-patient-per-year values were calculated for studied groups.

Hospital costs (inpatient medical care) included number of hospitalizations and days spent in hospital. It consisted of costs for hospital care (including medical materials), laboratory costs, EEG cost, neuroimaging cost and specialist consultations cost (by usual protocol at least psychologist, ophthalmologist, ear-nose-throat specialist).

Outpatient medical care costs included specialists consultations; paediatric neurologist, psychologist along with medical resources consumed. Great parts of outpatients' costs were diagnostics, mainly outpatient EEG and laboratory tests as plasma AED levels. Primary care consultation costs and costs attributable to epilepsy were not calculated.

AED treatment costs were calculated through accounting invoices. They were monitored by recording the initial hospital treatment and treatment changes during the study period to get total/cumulative quantities of every AED in milligrams. Total costs were calculated by multiplication of consumed quantities with price of daily defined dosage (DDD) by the NHS price list for the followed period[10]. The cost of AED treatment regarding modern and traditional drug groups was presented separately.

Lamotrigine, topiramate, vigabatrine and gabapentin made the modern AED group. The majority of the traditional group AED were valproic acid and carbamazepine.

Statistical analysis

Descriptive statistics was used to analyse the sample and specific patient subgroups. Student's t-test and analysis of the variance or nonparametric (Kruskal-Wallis or Mann-Whitney) tests, where appropriate, were used to test the significance of differences among groups. The children with unclassified epilepsy were excluded from the statistical analysis due to a few patients in sample.

Results

During the investigation period 88 children and adolescents were prospectively followed up for one year. Nineteen (19) children were excluded from the study due to residence outside UHC medical catchments or did not fulfil the ILAE criteria. Finally, 69 children and adolescents were included in the study. General characteristics of the patients are presented in the Table 1.

There were more males than females. The group of children aged 6–10 years included the most patients. Almost 60% of studied sample had partial epilepsy, with or without secondary generalization. It was not possible to determine the type of epilepsy for two children.

Preschool children were statistically significantly more frequently hospitalized (1.72), stayed longer in hospital (23.5 days) and had more outpatient consultations (5.39)

TABLE 1
GENERAL CHARACTERISTIC OF SAMPLE

Sex		N	%
	Male	40	57.9
	Female	29	42.1
Age			
	<= 5 years	18	24.6
	6–10 years	33	49.3
	11–18 years	18	26.1
Epilepsy syndrome			
	Partial epilepsy	41	59.4
1	Generalized epilepsy	26	37.7
	Unclassified epilepsy	2	2.9
Total		69	100.0

TABLE 2

HOSPITAL ADMISSIONS, DURATION OF STAY IN HOSPITAL AND SPECIALIST'S OUTPATIENTS VISITS BY STUDIED GROUPS

Age	Hospital admissions	Days in hospital	Outpatient consultations
<= 5 years	1.72 [a]	23.56[a]	5.39 [a]
6–10 years	1.09	9.03	3.12
11–18 years	1.06	7.11	3.39
Epilepsy syndrome	Hospital admissions	Days in hospital	Outpatient consultations
Partial epi.	1.37 [b]	13.39	3.90
Generalized epi.	1.04	9.81	3.73
Unclassified epi.[c]	1.50	23.00	2.00
General mean	1.25	12.32	3.78

Data expressed as mean per patient per year

a-p< 0.01, b-p<0,05, c-not included in statistical analyses

TABLE 3

ANNUAL COSTS PER PATIENT IN EUROS

Age	Hospital costs	Outpatients costs	AED-s costs	Total
<= 5 years	1 744.96 [a]	173.10[a]	391.03	2 290.87[a]
6–10 years	697.46	104.69	166.69	962.75
11–18 years	553.95	109.13	241.07[b]	889.49
Epilepsy syndrome	Hospital costs	Outpatients costs	AED-s costs	Total
Partial epi.	1 007.42	125.10	280.03	1 416.05
Generalized epi.	686.78	119.91	158.63	955.37
Unclassified epi.[c]	2 617.90	58.45	440.41	3 124.47
General mean	942.99	121.21	240.06	1 293.01

Values expressed as mean per patient per year

a-p< 0.01, b-p<0.05, c-not statistically calculated

than school children and adolescents, Table 2. There were not found differences between school children and adolescents through studied variables.

As seen in the table 2, the children and adolescents with partial epilepsy were significantly more frequently hospitalized (1.37) than those with generalized epilepsy. There was no difference regarding the duration of hospitalization and the number of outpatient visits regarding patients with generalized or partial epilepsy, Table 2.

Table 3 reports the mean annual cost per patient obtained from 12-month follow up in general and stratified to groups. The total annual cost per patient was 1 293.0 €.

In all groups combined, the highest annual cost were hospital admissions (942.99 €) followed by drug treatment (240.06 €) and outpatient specialist consultations (121.21 €). The main components of the total cost were ranked as follows: hospital admissions, AED treatment and outpatient visits respectively in all groups.

The preschool children had significantly the highest total annual costs per patient (2 290.87 €), as well as hospital costs (1 744.96 €) and outpatient medical interventions (173.10 €). Preschool children with epilepsy also had higher costs figures for drug treatment but not signi-

ficant in compare to the school-age children or adolescents. The only significant difference regarding the school-age children and adolescents was the cost of drug treatment. Drug treatment costs in adolescents were significantly higher than in school-aged children.

Considering epilepsy type, the highest cost was observed in the group of children with unclassified epilepsy. Due to a small number of patients with this entity, these data can only be illustrative. The children with partial epilepsy had higher total costs than the children with generalized epilepsy. It was the same regarding the costs per patient, hospital admissions, outpatient consultations and AED treatment, but it was not statistically significant.

Drug-consumption patterns are shown in the table 4. The most common prescription modality was monotherapy with traditional AED (70%). They made 35.3% of AED costs with the significantly lowest costs (122.03 €) of annual treatment. Twelve (12) patients (17%) with monotherapy consisting of modern AED represented 41.3% of AED costs, with the highest cost per-patient-per-year. Nine patients (13%) with combined traditional and modern AED polytherapy represented 23.2% of AED costs. The last mentioned group had substantial expenditures

TABLE 4
ANTIEPILEPTIC DRUGS (AED) COSTS REGARDING TRADITIONAL AND MODERN ANTIEPILEPTICS AND THEIR PROPORTIONS

AED	No. Patients	Costs per patient per year / €	% of AED cost
Traditional	48 (70%)	122.03 [a]	35.3%
Modern	12 (17%)	571.24	41.3%
Traditional + Modern	9 (13%)	427.97	23.2%
TOTAL	69 (100%)	240.06	100.0%

a-p< 0.01, In brackets percentage of patients

of annual treatment and no significant difference in expenditure between costs for modern monotherapy treatment.

Distributions of costs by used resources are shown in Figure 1. Hospital treatment was the highest consumer of assets (72%), followed by AED treatment (19%). Outpatient visits represent only 9% of costs of all used resources.
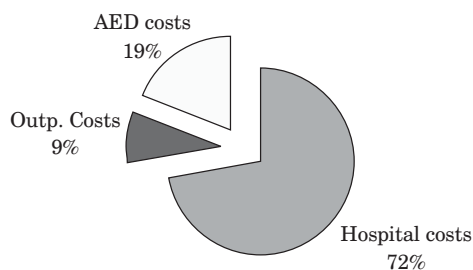

Fig. 1. Distributions of costs by used resources. AED- anti epileptic drugs, Outp.Costs- outpatients costs.

Discussion

Our study was performed following the general recommendations regarding direct economic costs of epilepsy[11,12]. Still, it can be compared with rather limited investigations due to scarce published reports regarding childhood age[4–7].

Guerrini et al. calculated the cost of childhood epilepsy in Italy regarding health care setting[5]. In that study the mean annual cost per epilepsy patient was 1 767 € and the highest cost was in newly diagnosed cases at the teaching hospital, 2 660 €. The cost of epilepsy in European countries varies from 900 € to 3 000 € per-patient-per- year for active cases[13,14]. The average cost per patient in our study was 1 297 €, similar to developed countries. The overall regional or intra-regional development create diverse economic circumstances, which might cause difficulties in comparison or peer faced interpretation[5,6,7].

We found that in our settings hospitalizations were both longer (average 12.3 days) and had more frequent (average 1.25) comparing to western countries[5,14,15]. Rather predictably, hospital costs represented greater relative share (72%) of consumed resources. This result is in

line to the most of epilepsy costs studies, whether children or adults populations[16,17,13].

Differences among studies might be explained by the discrepancies in terms of unit costs. The most important proportion in majority of studies were hospital admission costs, followed by drug consumption and outpatient services[13]. In Croatia, i.e. in our study, unit costs are defined by medical insurance provider[9,10]. Therefore it should be considered when compared with cost-benefit, cost-effectiveness or cost-minimalisation studies. Hospital costs in studies varied and depended both on the organization and financing of health care settings.

Our results clearly show that costs significantly vary regarding the child's age when epilepsy started. The younger was the child, the costs were higher. Preschool children (≤ 5 years) had statistically significantly higher costs in all the studied parameters. The annual cost per patient in children under 5 years was 2 290 €, almost double to general mean and 2.5 times more than in school-aged children or adolescents. Similarly, costs were also found higher in regard to AED consumption and outpatients' visits.

Cost variation in patients with epilepsy might be the result of epilepsy type[18]. Guerrini at all showed that cost of epilepsy varies significantly with severity of disease, its temporal stage and its response to treatment[5,19]. In our study we did not find any significant difference in costs regarding partial and generalized epilepsies. We presume that in our study the infants with West syndrome, who were more frequently hospitalized and had longer hospitalization duration, increased the costs for the entire generalized epilepsy group. The highest costs were observed within unclassified epilepsy, but this result may be only illustrative due to a small number of patients.

Epilepsy is heterogeneous clinical condition, therefore the classification into partial, generalized and unclassified type is relatively crude yardstick. A relatively small number of cases in defined syndromes is an exception and reacts unpredictably. Additional challenge to find more accurate economic burden of epilepsy is to calculate the cost of epilepsy regarding the classification in syndromes. It might modify the evidence that showed the highest costs of drug resistant epilepsy.

Drug treatment made 19% of overall costs in our study, figure 1. This finding should be explained with caution. Most of published cost studies cannot be com-

pared due to different methodological approaches[20]. On one hand, our result corresponds to many studies performed in western countries, which showed that the second source of direct costs of epilepsy are AED[13]. On the other hand, we showed that the traditional AED represents a common prescription routine in Croatia, except in children with modern AED, representing approximately 30% of all AED used[21]. Seventy percent (70%) of our children were treated with traditional AED which represented only 1/3 of total AED cost, table 4. Modern AED may represent a significant burden in the direct medical cost of epilepsy[22,23,24]. Four new generation AED were approved and are available in Croatia: lamotrigine (LTG) in 1995, viagabatrine (VGB) in 1997, topiramate (TPM) in 1998 and gabapentine (GBP) in 2002. In our study, 12 children treated with modern AED accounted for 40,4% of the entire treatment cost. Our findings are related to childhood and adolescence epilepsy treatment and biase from the general population with epilepsy in Croatia[25]. Moreover, the mean annual treatment cost per patient in our study (240 €) was higher compared to the results from Italy study (185 €)[5]. Such findings may result from the study at the university settings[5,26].

To the best of our knowledge this is the first study regarding the costs of epilepsy in Croatia. Direct medical cost of epilepsy in Croatian children and adolescents re-

garding the annual cost per person, costs of resource consumed or cost distribution of AED are reasonably comparable to those on the international level. In this manner it would be difficult to make fair compare or appraise concerning other chronic diseases in childhood due to substantial differences in patophysiology, natural course or temporal response to treatment. One must not disregard both study settings and regional-external influences when trying to draw conclusions from published literature.

Costs of epilepsy in our settings depended mostly on the age when the disease appeared – the younger was the child, the costs were higher. We did not in-calculate primary care costs, thus the annual costs might be even higher.

Economic aspects of disease-treatment analysis must insure benefits for patients, health care providers and general health policy. In countries with new rising systems, limited resources assigned to the health care settings demand rational allocation of the available funds. Analyzing and reanalyzing the costs is the constant need due to numerous options in diagnosis and treatment of epilepsy. Cost-of-illness evaluation might be defined as a creative process. All expenditure should be clearly defined and pointed out for discussion.

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IZRAVNI MEDICINSKI TROŠKOVI DIJAGNOSTIKE I LIJEČENJA EPILEPSIJE DJECE I ADOLESCENATA

S A Ž E T A K

Cilj istraživanja bio je utvrditi izravne medicinske troškove epilepsija u djece i adolescenata te utvrditi utjecaj tipa epilepsije i dobi oboljelog djeteta na sveukupne troškove liječenja. Provedena je jednogodišnja prospektivna analiza šezdeset i devetero djece (69) oboljelih od epilepsije (po kriterijima Međunarodne lige za brobu protiv epilepsije).Izravni medicinski troškovi izračunati su sumiranjem godišnjeg troška hospitalizacije, ambulantnih obrada i primjene antiepileptika. Srednja vrijednost godišnjeg troška po pacijentu iznosila je 1293,0 €. Troškovi hospitalizacije iznosili su 942,9 € (72%),troškovi terapije antiepilepticima 240,0 € (19%), a troškovi ambulantne obrade 121,2 € (9%). Sveukupni troškovi značajno su viši za djecu dobi ispod 5 godina. Troškovi liječenja antiepilepticima značajnije su niži u skupini djece liječene tradicionalnim antiepilepticima (€122,0) u usporedbi sa djecom liječenom modernim antiepilepticima (571,2€). Troškovi liječenja epilepsije u djece i adolescenata u Hrvatskoj sukladni su onima u razvijenim zemljama. Troškovi značajno variraju u ovisnosti o dobi djeteta. Evaluacija troškova liječenja bolesti važan su prvi korak prema racionalnoj uporabi dostupnih resursa.